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Preliminary communication

Glycosylation of 1,2-*O*-cyanoethylidene derivatives of carbohydrates

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The synthesis of polysaccharides containing oligosaccharide repeating units has been accomplished by polycondensation of suitable monomers, namely, trityl ethers of 1,2-*O*-(1-cyanoethylidene) derivatives of the respective oligosaccharides[1–3]. These monomers were prepared from 1,2-*O*-(1-cyanoethylidene) derivatives of oligosaccharides, which, in turn, were obtained by the reaction of acetylated glycosyl bromides with silver cyanide in boiling xylene[4] (Coxon–Fletcher procedure[5]) or with sodium (or potassium) cyanide in acetonitrile[2,6]. As part of our study of the synthesis of heteropolysaccharides, we have examined an alternative approach to 1,2-*O*-cyanoethylidene derivatives of oligosaccharides, namely, glycosylation of monosaccharide 1,2-*O*-cyanoethylidene derivatives which are themselves glycosylating agents (*cf.* ref. 2), and now report the preparation of some disaccharide 1,2-*O*-cyanoethylidene derivatives by this approach.

Two types of monosaccharide cyanoethylidene derivatives were employed, containing free hydroxyl groups or a trityl group. The former were glycosylated by using acylglycosyl bromides under Helferich conditions (acetonitrile, mercuric cyanide), and the latter using sugar 1,2-thio-orthoesters.

Interaction of the diol **1** {m.p. 108–108.5° (from chloroform), $[\alpha]_D^{20}$ +12.5° (*c* 2.5, chloroform), obtained by Zemplén deacetylation of the corresponding diacetate[7]} with 2,3,4-tri-*O*-acetyl-α-L-rhamnopyranosyl bromide (1.4 equiv.) afforded disaccharide derivatives **2** and **3*** (Table I) along with a trisaccharide derivative (14%). Identical products were obtained on benzoylation of **3** and rhamnosylation of **4** {m.p. 108.5–109.5° (from ether–hexane), $[\alpha]_D^{20}$ −13° (*c* 2.6, chloroform), prepared by selective benzoylation of **1**}.

Analogous glycosylation of **1** using 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl bromide followed by acetylation gave the disaccharide derivatives **5**–**7** together with a trisaccharide derivative (4%). Glucosylation of the 4-acetate of **1** afforded **5** and **6** in the ratio ~4:1 (^{13}C-n.m.r. data; total yield, 36%). Disaccharides **8** and **9** (ratio ~2:3; total yield, 37%) were obtained from **4**.

*All new compounds gave correct C, H, and N analyses, and the ^{1}H- and ^{13}C-n.m.r. spectra were in accord with the structures assigned.

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1 $R^1 = R^2 = H$

2 $R^1 = \alpha$-RhoAc$_3$, $R^2 = H$

3 $R^1 = H, R^2 = \alpha$-RhoAc$_3$

4 $R^1 = Bz, R^2 = H$

5 $R^1 = \alpha$-GlcAc$_4$, $R^2 = H$

6 $R^1 = \beta$-GlcAc$_4$, $R^2 = H$

7 $R^1 = A^1, R^2 = \alpha,\beta$-GlcAc$_4$

α,β-[illegible]

8 $R^1 = Bz, R^2 = \alpha$-GlcAc$_4$

9 $R^1 = Bz, R^2 = \beta$-GlcAc$_4$

17 $R^1 = Tr, R^2 = A^1$

10 $R^1 = R^2 = H$

12 $R^1 = \alpha$-RhoAcBz$_2$, $R^2 = H$

13 $R^1 = H, R^2 = \alpha$-RhoAcBz$_2$

14 [illegible]

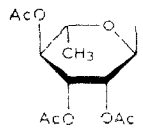
16 $R^1 = \beta$-[illegible] $= Bz$

18 $R^1 =$ [illegible]

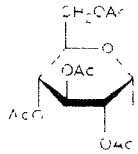
19 [illegible]

20 [illegible]

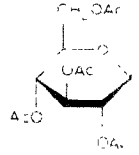
α-RhoAc$_3$ =



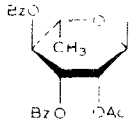
α-GlcAc$_4$ =



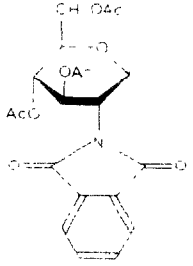
β-GlcAc$_4$ =



α-RhoAcBz$_2$ =



β-[illegible]



Attempted Koenigs–Knorr glucosylations of **1** and **4** (dichloromethane, silver oxide) failed; each starting cyanoethylidene derivative was recovered in almost quantitative yield.

Glycosylation of the diol **10**[8] resembled that of **1**; **10** with 1 equiv. of 2-*O*-acetyl-3,4-di-*O*-benzoyl-L-rhamnopyranosyl bromide (**11**) yielded the disaccharide derivatives **12** and **13**, together with a trisaccharide derivative (4%); 31% of **10** was recovered. Compound **11** was prepared by the sequence 3,4-di-*O*-benzoyl-1,2-*O*-benzylidene-β-L-rhamnopyranose[9] → 3,4-di-*O*-benzoyl-L-rhamnopyranose (m.p. 137–145° (from chloroform–hexane), $[\alpha]_D^{20}$

TABLE I

PROPERTIES OF THE 1,2-*O*-CYANOETHYLIDENE DERIVATIVES OF DISACCHARIDES

Compound	*Isolated yield (%)*	*M.p. (deg.) (solvent)*	$[\alpha]_D^{20}$ *(deg.) (c, $CHCl_3$)*	*^{13}C-N.m.r. data (chemical shifts in p.p.m.; $CDCl_3$)*						
				C-1'	*C_{Gl}[a]*	*C-1*	*C-2*	*CH_3—C———CN*		
2	39	Amorphous	−37 (1)	97.4	76.4	97.0	75.7	25.4	99.1	116.7
3	22	173–174 (abs. ether)	−32 (1.2)	99.3	78.3	96.6	76.8	24.9	99.6	117.0
5	9	Amorphous	+68 (1)	96.8	75.2	96.8	74.4	25.1	99.6	116.6
6	29	169.5–170.5 (abs. ether–hexane)	−7 (1.6)	100.8	75.0	95.9	74.2	25.1	100.0	116.6
7	18	Amorphous	+10.5 (1.2)	102.2	76.7	97.1	73.6	24.2	99.6	[b]
8	37	205.5–206.5 (abs. ether)	+61 (1)	95.0	72.5	96.5	73.9	24.6	100.0	116.5
9		Syrup	−13 (2)	102.3	76.8	97.2	73.9	24.3	99.8	116.5
12	41	Amorphous	+31 (2.2)	100.5	81.1	96.8	80.5	26.6	101.5	117.1
13	22	Amorphous	+14 (1.6)	99.2	79.5	97.0	81.2	26.4	101.0	117.0
15	90.5	92–94 (ether–ethyl acetate–hexane)	+29 (1.8)	100.6	78.5	96.7	80.8	26.5	101.4	117.0
16	65	209–210 (ethanol)	+47.5 (1.6)	99.8	77.9	96.6	80.6	26.3	101.0	116.7
18	37	197–198.5 (methanol)	+102.5 (0.7)	100.3	78.3	96.9	80.3	26.5	101.8	117.0

[a] C_{Gl} denotes the glycosylated carbon atom. [b] Chemical shifts of the major (1→4)-β-linked disaccharide are given; the CN signal was of low intensity.

+44° (equil.; *c* 1.6, chloroform)} → 1,2-di-*O*-acetyl-3,4-di-*O*-benzoyl-L-rhamnopyranose {$[\alpha]_D^{20}$ +36° (*c* 2.4, chloroform)} → **11**. With 1.5 equiv. of the glycosylating agent, **10** gave 10.5% of the trisaccharide derivative, but the yields of **12** and **13** were unchanged and 10% of **10** was recovered.

The reaction (Helferich conditions) of **11** and 3,4,6-tri-*O*-acetyl-2-deoxy-2-phthalimido-D-glucopyranosyl bromide[10] (1.5 equiv.) with **14** gave the disaccharide derivatives **15** and **16** in high yield. The glycosyl acceptor **14** was prepared as follows from methyl 2,3-*O*-isopropylidene-α-L-rhamnopyranoside. Conventional benzylation followed by hydrolysis gave 4-*O*-benzyl-L-rhamnose {m.p. 138–141° (from ethyl acetate), $[\alpha]_D^{20}$ −38.5° (equil.; *c* 1, methanol)}. Acetylation then afforded 1,2,3-tri-*O*-acetyl-4-*O*-benzyl-α-L-rhamnopyranose {m.p. 101–102° (from ether–hexane), $[\alpha]_D^{20}$ +18° (*c* 1.5, chloroform)}, which gave the glycosyl bromide with hydrogen bromide–dichloromethane. Treatment[6] with sodium cyanide in acetonitrile then yielded a mixture of 3-*O*-acetyl-4-*O*-benzyl-1,2-*O*-[1-(*exo*- and *endo*-cyano)ethylidene]-β-L-rhamnopyranoses in the ratio 4.3:1 (^{1}H-n.m.r. data). The *exo*-CN isomer {m.p. 122–124° (from ether–hexane), $[\alpha]_D^{20}$ +26° (*c* 2.3, chloroform)} was deacetylated to give **14**, m.p. 119–120° (from ether–hexane), $[\alpha]_D^{20}$ −16° (*c* 1.3, chloroform).

Glycosylation of trityl ethers of 1,2-*O*-cyanoethylidene derivatives by 1,2-thioorthoesters of monosaccharides under conditions previously described[11] (CH_2Cl_2, triphenylmethylium perchlorate as catalyst) was less effective than glycosylation under Helferich conditions, probably because of the instability of the cyanoethylidene group.

Treatment of **17** {m.p. 144–145° (from ether–hexane), $[\alpha]_D^{20}$ −39° (*c* 2, chloroform)} with 3,4,6-tri-*O*-acetyl-1,2-*O*-[1-(*exo*-ethylthio)ethylidene]-α-D-glucopyranose[12] gave **5** and **6** in yields of 10 and 12%, respectively, and 10% of **17** was recovered. The trityl ether **17** was obtained by selective tritylation[13] of **1** by triphenylmethylium perchlorate to afford the 3-*O*-trityl derivative {m.p. 123–124° (from ether–hexane), $[\alpha]_D^{20}$ −64° (*c* 1.3, chloroform)} followed by acetylation.

The disaccharide derivative **18** (37%) was obtained by condensation of the trityl ether **20** {$[\alpha]_D^{20}$ +24° (*c* 1, chloroform), obtained by benzoylation of **19**[8]} with 3,4-di-*O*-benzoyl-1,2-*O*-[1-(*exo*-*p*-tolylthio)ethylidene]-β-L-rhamnopyranose {m.p. 125–127°, $[\alpha]_D^{20}$ +159° (*c* 2, chloroform)}, obtained from the corresponding 3,4-diacetate[14] by deacetylation in the presence of pyridine[15] followed by benzoylation. The same disaccharide derivative was also prepared by benzoylation of **12**.

Thus, glycosylation of 1,2-*O*-cyanoethylidene derivatives of monosaccharides is established as a new route to 1,2-*O*-cyanoethylidene derivatives of oligosaccharides.

REFERENCES

1 I. V. Obruchnikov and N. K. Kochetkov, *Tetrahedron Lett.*, (1977) 57–60.
2 N. K. Kochetkov, V. I. Betaneli, M. V. Ovchinnikov, and L. V. Backinowsky, *Tetrahedron*, 37, Suppl. 9 (1981) 149–156.
3 N. K. Kochetkov and E. M. Klimov, *Tetrahedron Lett.*, (1981) 337–340.

4 I. V. Obruchnikov and N. K. Kochetkov, *Izv. Akad. Nauk SSSR, Ser. Khim.*, (1977) 2571–2574.
5 B. Coxon and H. G. Fletcher, Jr., *J. Am. Chem. Soc.*, 85 (1963) 2637–2642.
6 V. I. Betaneli, M. V. Ovchinnikov, L. V. Backinowsky, and N. K. Kochetkov, *Carbohydr. Res.*, 68 (1979) C11–C13.
7 V. I. Betaneli, M. M. Litvak, L. V. Backinowsky, and N. K. Kochetkov, *Carbohydr. Res.*, 94 (1981) C1–C4.
8 N. K. Kochetkov and N. N. Malysheva, *Tetrahedron Lett.*, (1980) 3093–3096.
9 V. I. Betaneli, M. V. Ovchinnikov, L. V. Backinowsky, and N. K. Kochetkov, *Carbohydr. Res.*, 107 (1982) 285–291.
10 R. U. Lemieux, T. Takeda, and B. Chung, *Am. Chem. Soc., Symp. Ser.*, 39 (1976) 90–115.
11 L. V. Backinowsky, Yu. E. Tsvetkov, N. F. Balan, N. E. Byramova, and N. K. Kochetkov, *Carbohydr. Res.*, 85 (1980) 209–221.
12 N. K. Kochetkov, L. V. Backinowsky, and Yu. E. Tsvetkov, *Tetrahedron Lett.*, (1977) 3681–3684.
13 V. I. Betaneli, M. V. Ovchinnikov, L. V. Backinowsky, and N. K. Kochetkov, *Carbohydr. Res.*, 76 (1979) 252–256.
14 L. V. Backinowsky, Yu. E. Tsvetkov, N. E. Byramova, N. F. Balan, and N. K. Kochetkov, *Izv. Akad. Nauk SSSR, Ser. Khim.*, (1980) 1905–1911.
15 L. V. Backinowsky, N. E. Byramova, Yu. E. Tsvetkov, and V. I. Betaneli, *Carbohydr. Res.*, 98 (1981) 181–193.